

provided by a combination of carbonate and at least one of bicarbonate and citrate.--

Add the following new claim:

--26. (new) The composition according to claim 3, wherein the weight ratio of phosphorus to creatine is about 1:6 to about 1:4.

Please charge the fee of \$18 for the one extra dependent claim added herewith, to Deposit Account No. 25-0120.

REMARKS

The claims are revised as to form, to address the claim objections set forth at page 2 of the Official Action.

The rejection of claim 3 for indefiniteness is overcome by deleting from that claim the narrower preferred range. We note that the narrower preferred range is made the subject of the new dependent claim 26.

At pages 3-4 of the Official Action, claims 1-5, 10, 11, 13, 14, 16-19, 21, 22 and 25 were rejected as allegedly being anticipated by, or, alternatively, obvious in view of SIMONE 5,397,786. Those rejections are respectfully traversed, for the following reasons.

SIMONE describes a rehydration drink that contains at least one carbohydrate, at least one electrolyte, at least one ammonia neutralizer, at least one energy enhancer, at least one antioxidant, at least one neuromuscular enhancer, at least one membrane stabilizer and water.

The electrolytes may be selected from a great variety of salts (column 2, line 64-column 3, line 18). Table 1 provides preferred amounts of electrolytes. SIMONE describes that Drink A preferably contains 200 mg K_3PO_4 and 300 mg Na_3PO_4 (Table 1), which corresponds to 86 mg P, which in turn corresponds to about 12% of the daily recommended intake of phosphorus. Drink B preferably contains 40 mg K_3PO_4 and 40 mg Na_3PO_4 (Table 1), which corresponds to 13 mg P, which in turn corresponds to about 2% of the daily recommended intake of phosphorus.

SIMONE gives in Table 1 numerous variations for composing the electrolyte part of the drinks. Even the highest amounts of phosphate salts in a drink as described by SIMONE, i.e. 2000 mg K_3PO_4 (see Table 1), provides only 41% of the daily recommended intake of phosphorus; moreover, this high amount is not a realistic anticipatory disclosure of SIMONE, in view of his preferred maximum of 1,000 mg of electrolytes (all electrolytes) in column 3, lines 19-20.

The present invention relates to a composition containing at least 75% of the daily recommended intake of phosphorus per serving. Thus, SIMONE does not anticipate applicants' invention, since SIMONE does not disclose a composition that falls within the scope of applicants' invention.

Applicants also respectfully disagree with Examiner's opinion that based on SIMONE alone the skilled artisan would somehow arrive at the claimed invention.

SIMONE describes a rehydration drink that contains, at least one carbohydrate, at least one electrolyte, at least one ammonia neutralizer, at least one energy enhancer, at least one antioxidant, at least one neuromuscular enhancer, at least one membrane stabilizer and water.

SIMONE describes that the electrolytes preferably are salts of a metal of the Group I and II of the Periodic System, preferably inorganic and organic salts of sodium, potassium, calcium and/or magnesium (column 2, line 66-column 3, line 2). Several examples of such salts are given (column 2, lines 2-14). SIMONE does not disclose or give any hint towards the advantageous effects of including a particular anionic group in the electrolyte salt composition, nor does SIMONE give any hint as to the improvements that can be expected from choosing phosphorus containing salts. Hence, the skilled artisan would not suspect from SIMONE that the inclusion of phosphorus in an amount of at least 75% of the daily recommended intake would have an advantageous effect.

Furthermore, SIMONE describes that the electrolytes are present in amounts of 2 to 2500 mg (column 3, lines 18-19). SIMONE thus clearly describes that the inclusion of electrolytes is bound to an upper limit, i.e. 2500 mg electrolyte. SIMONE does not give any indication to select a single electrolyte salt for inclusion in the drink, nor does SIMONE give any indication towards the advantageous effects of inclusion of phosphorus

containing salts. Thus, by including 2500 mg of a phosphorus containing electrolyte salt in the drink described by SIMONE, the skilled man would deviate from the teaching of SIMONE. However, even in the case where the skilled man would deviate from the teaching by SIMONE through including 2500 mg of one of the described phosphate salt in the drink, i.e. 2500 mg K_3PO_4 or 2500 mg Na_3PO_4 , this would still not result in the composition containing at least 75% of the daily recommended intake of phosphorus.

Moreover, with the indication that the inclusion of the specified electrolyte salts is bound to an upper limit (i.e. 2500 mg, column 3, lines 18-19), which inevitably leads to a phosphorus content below the lower limit described by the applicants, SIMONE even teaches away from the invention.

Hence, applicants respectfully submit that a person of ordinary skill, based on SIMONE would not arrive at applicants' invention, nor would such person suspect from SIMONE that the administration of creatine, at least 75% of the daily recommended intake of phosphorus per serving and blood buffer gives an unexpected improvement in the anaerobic working capacity. Hence, applicants respectfully submit that the invention is both novel and unobvious over SIMONE.

At pages 4-6 of the Official Action, all of the pending claims 1-22 were rejected as allegedly being unpatentable, within the meaning of 35 USC §103(a), based on the proposed combination

of SIMONE in view of WEINSTEIN et al. 6,013,290, WO 96/04240, FANG 5,886,040, Webster's Dictionary (10th Edition), ODIAN et al. (Schaum's Outline), HULTMAN et al. 5,767,159 and ST. CYR et al. 6,159,942. That rejection is also respectfully traversed, for the following reasons.

The eight references cited do not contain any explicit or implicit motivation to be combined. Hence, the documents can only be combined with the benefit of hindsight. Applicants therefore respectfully disagree with the obviousness rejection, since the skilled artisan, without any foreknowledge of the invention would not have had any motivation to arrive at the claimed invention.

Furthermore, applicants disagree with Examiner's opinion that based on a combination of two or more of the eight references the skilled artisan would arrive at the claimed invention.

The cited references do not relate to the problems or improvements relating to combinations of creatine and relatively high amounts of phosphorus per serving, nor do the cited references alone or in combination suggest that blood buffer possesses the capability to counteract the adverse effects of administration of creatine and at least 75% of the daily recommended intake of phosphorus.

WEINSTEIN et al. disclose a nutrient drink to prevent fluid loss. They also describe that citrate can be used for increasing the alkaline reserve in blood to counter the increased acidity of exercise, which contributes to fatigue (column 5, lines 50-58). The main goals of nutrient beverage formulations as provided by WEINSTEIN et al. are to prevent fluid loss by ingestion of fluids, maintain proper levels of electrolytes and increase carbohydrates in the body prior to exercise (column 2, lines 34-42).

WEINSTEIN et al. disclose that other agents may be included in the formulations, which may or may not have positive effects (column 6, lines 19-23). The skilled artisan might learn from this disclosure that appropriate levels of water in the body are important for body performance. However, the skilled man would not be able to make any sensible selection from the list of optional agents, particularly because WEINSTEIN et al. explicitly mention that optional components such as phosphates may or may not have positive effects. SIMONE does not give any hint as to the necessity to include phosphate salts in the composition. SIMONE only describes that the electrolytes preferably are salts of a metal of the Group I and II of the Periodic System, preferably inorganic and organic salts of sodium, potassium, calcium and/or magnesium. Absent a hint towards the essentiality of phosphate salts by SIMONE, and the lack of certainty of that phosphates would give any advantageous effects, the skilled

artisan would at least have serious doubts towards the necessity to include phosphates in a formulation.

Even if the skilled artisan would choose to include phosphate salts in the formulation as described by WEINSTEIN et al., he would use SIMONE as guidance for the amounts of phosphate salts to be included in the formulation. Hence, the skilled man would choose the preferred amounts as described by SIMONE (see Table 1). The preferred amounts of electrolytes described by SIMONE are underlined in Table 1 (see column 4, lines 28-30). Drink A preferably contains 200 mg K_3PO_4 and 300 mg Na_3PO_4 (Table 1), which corresponds to 86 mg P, which in turn corresponds to about 12% of the daily recommended intake of phosphorus, Drink B preferably contains 40 mg K_3PO_4 and 40 mg Na_3PO_4 (Table 1), which corresponds to 13 mg P, which corresponds to about 2% of the daily recommended intake of phosphorus.

Even if the skilled artisan would choose to include the highest amounts of phosphate salts in a drink as described by SIMONE, i.e. 2000 mg K_3PO_4 (see Table 1), the serving would still only provide about 41% of the daily recommended intake of phosphorus. In conclusion, the skilled man would not arrive at a composition comprising creatine, at least 75% of the daily recommended amount of phosphorus per serving and blood buffer by combining SIMONE and WEINSTEIN et al. Even in retrospect, all elements of the invention cannot be found in WEINSTEIN et al. and SIMONE, nor would a skilled man find any hint as to the

advantageous effects of the combined creatine, at least 75% of the daily recommended intake of phosphorus per serving and blood buffer.

WO 96/04240 (NEGRISOLI et al.) relates to hydrosoluble creatine in water and methods for the preparation of hydrosoluble creatine salts. The document does not teach a composition comprising creatine and phosphorus. The document thus does not give the skilled person any hint as to improvements relating to the combination of creatine and relatively high amounts of phosphorus. Applicants respectfully disagree that NEGRISOLI et al. can provide any basis for obvious rejection, alone or in combination with other documents.

FANG relates to the creatine pyruvate. Creatine pyruvate is described in the document as a solution to the problem of limited palatability of pyruvate and creatine alone. FANG does not teach a combination of creatine and phosphorus, a combination of creatine and blood buffer, or a combination of phosphorus and blood buffer. Additionally, FANG does not teach a combination of creatine, phosphorus and blood buffer, nor does FANG provide any teaching as to the advantageous inclusion of blood buffer in a composition comprising a combination of creatine and at least 75% of the daily recommended intake of phosphorus.

Furthermore, FANG relates to the problem of reduced palatability of compositions containing creatine and pyruvate.

The skilled person would thus not consult this document when attempting to improve body performance via food supplements containing creatine, however, may use this document to improve palatability of compositions containing creatine and pyruvate.

FANG thus cannot provide any basis for obvious objections, alone or in combination with other documents.

Webster Dictionary (10th Edition) is cited as disclosing the definition of "precursor". Applicants believe this disclosure provides no support to the rejection of the present claims.

ODIAN et al. describe the Krebs cycle. ODIAN et al. however are not concerned with improvements of body performance nor with compositions containing creatine, phosphorus and blood buffer. Therefore, this document likewise lacks relevance to the present invention.

HULTMAN et al. describe a method for increasing the muscle performance capability in mammals by administering to the mammal at least 15 grams creatine. HULTMAN et al. explain their view on the intracellular function of creatine phosphate (column 1, lines 22-30). This does thus not in any manner relate to oral administration of creatine phosphate. In fact, HULTMAN et al. teach that phosphocreatine can hardly be used in a therapeutic situation, as it cannot pass the cell membrane (column 2, lines 48-49). Additionally, HULTMAN et al. do not teach that the administration of phosphorus with creatine provides advantageous

effects. The lack of a recommendation to advantageously combine phosphorus and creatine and the recommendation to exclude phosphocreatine from a preparation for improvement of body performance even teaches away from the combination of creatine and at least 75% of the daily recommended value of phosphorus and thus does not in any manner relate to a combination of creatine, at least 75% of the daily recommended value of phosphorus per serving and blood buffer.

In conclusion, this disclosure fails to provide any hint towards the claimed invention.

ST. CYR et al. describe methods for increasing the energy levels of healthy humans by orally administering an effective amount of a pentose to said human, optionally combined with creatine. The document does not provide a combination of creatine and phosphorus, creatine and blood buffer or blood buffer and phosphorus, nor does it suggest to combine a blood buffer in a composition comprising a combination of creatine and at least 75% of the daily recommended intake of phosphorus and creatine. Thus, it is believed that this document, alone or in combination, cannot provide a basis for an obviousness rejection.

In summary, the selected prior art may contain bits and pieces that can be used to construct the invention, but the selection of the prior art and the construction of the invention can only be made with the benefit of having knowledge of the invention, and is thus unsuitable for an obviousness assessment.

UNEXPECTED RESULTS

As disclosed by the applicants, power output can be improved using creatine and/or phosphorus. Creatine provides an improvement in power output of 3%, administration of phosphorus improves the power output by 3% and the combination of creatine and phosphorus and creatine improves the power output by 6% (specification, page 10, Table 1). Applicants found that administration of creatine and blood buffer improved anaerobic working capacity 15.6% and that coadministration of creatine, at least 75% of the daily recommended dosage of phosphorus per serving and blood buffer markedly improved the anaerobic working capacity with 49.8% (see specification, page 18, Table 2), which is the result of a surprisingly synergistic and unexpected effect (see page 8, line 4).

These tests, both inside and outside the range of applicants' invention, show the criticality of the inclusion of blood buffer in a composition containing creatine and at least 75% of the daily recommended value of phosphorus per serving. The unexpected and synergistic results of the invention are thus sufficiently established. The presence of these results that are greater than expected are evidence of non-obviousness (MPEP 716.02).

As the Examiner is aware, when the specification itself contains evidence of unexpected results, this must be accorded the same weight as a Rule 132 declaration, and must be considered

in the first instance in assessing whether the prior art makes out a *prima facie* case of obviousness (*In re Wright*, 6 USPQ2d 1959 (Fed. Cir. 1988)).

Additionally, it is respectfully pointed out that based on the above cited references, the skilled artisan would not conclude that ingestion of creatine, at least 75% of the daily recommended value of phosphorus per serving and blood buffer would provide an improvement in anaerobic working capacity of about 50%. In fact, the references cited are silent on improvements of anaerobic working capacity (AWC) with combinations of creatine, phosphorus and blood buffer.

The absence of any hint towards the improvement of AWC with a combination of creatine, at least 75% of the daily recommended value of phosphorus per serving and blood buffer and the marked synergistic improvement of AWC due to the ingestion of the novel composition according to applicants' invention thus overcome the *prima facie* obviousness rejection.

From the above discussion, it is apparent that applicants' invention is novel and non-obvious over SIMONE, alone or in view of the other cited references. Favorable reconsideration and withdrawal of the prior art rejections are therefore respectfully requested.

In view of the present amendment and the foregoing remarks, therefore, it is believed that this application has been placed in condition for allowance, with claims 1-26, as amended.

STOUT et al. S.N. 09/769,245

Allowance and passage to issue on that basis are accordingly respectfully requested.

Attached hereto is a marked-up version showing the changes made to the claims. The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE."

Respectfully submitted,

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"VERSION WITH MARKINGS TO SHOW CHANGES MADE"

IN THE CLAIMS:

Claim 1 has been amended as follows:

--1. (amended) A composition comprising:

[a.] creatine;

[b.] a phosphorus supplement, wherein the phosphorus supplement provides at least 75% of the recommended daily dose of phosphorus value per serving; and

[c.] a blood buffer.--

Claim 3 has been amended as follows:

--3. (amended) The composition according to claim 1, wherein the weight ratio of phosphorus to creatine is about 1:10 to about 1:1[, preferably about 1:6 to about 1:4].--

Claim 9 has been amended as follows:

--9. (twice amended) The composition according to claim 7, wherein the organic creatine salt further comprises an anionic component selected from the group consisting of tartrate, maleate, malate, fumarate, citrate, and pyruvate.--

Claim 12 has been amended as follows:

--12. (twice amended) The composition according to claim 9, wherein the anionic component of the organic creatine salt is a precursor of a Krebs cycle intermediate.--

Claim 14 has been amended as follows:

--14. (twice amended) The composition according to claim 1, comprising 1-10 [gram] grams of creatine, 0.6-5 [gram] grams of phosphorus, 0.5-15 [gram] grams of said blood buffer, and further comprising 1-100 g of digestible carbohydrates.--

Claim 21 has been amended as follows:

--21. (amended) [A] The method according to claim 18, wherein the subject is human.--

Claim 22 has been amended as follows:

--22. (amended) [A] The method according to claim 21, wherein the subject is male.--

Claim 23 has been amended as follows:

--23. (amended) The composition according to claim 14, wherein the creatine is provided by creatine citrate, the phosphorus is provided by phosphate, and the blood buffer is provided by a combination of carbonate and at least one of [biocarbonate] bicarbonate and citrate.--